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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/652,604	08/30/2000	Robert C. Spiro	07078-032001	3029

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EXAMINER
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MAYES, LAURIE A

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/652,604

Applicant(s)

SPIRO ET AL.

Examiner

Laurie Mayes

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 8-18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8-18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____.  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other:  |

### DETAILED ACTION

Applicant's arguments filed on June 30, 2003 have been fully considered but they are not persuasive.

#### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-6, 8, 10 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Cook et al. Cook et al. teach a biodegradable (col. 5, line 29) matrix comprised of two layers (col. 5, lines 30-45) comprising a polymeric component consisting of a protein and a polysaccharide wherein the protein is albumin (Example 26, col. 24, lines 35-40) and the polysaccharide is selected from the group consisting of dextran, alginate, hyaluronic acid (claim 7, col. 26, lines 54-59) and heparin (Ex. 24, col. 24, line 19) and the protein is albumin, (Ex. 26), and wherein: said protein and/ or polysaccharide are cross-linked to each other with glutaraldehyde (Example 3, col. 17, lines 35-40); said layers are different in composition from each other (polyethyleneimine and polylysine, Ex. 6, col. 18, lines 35-40); said layers attach to each other through chemical cross-linking (col. 9, lines 43-50); one layer is more porous than the other (Ex. 16, col. 21, lines 57-58) and wherein the matrix contains the growth factor rhBMP-2 (Ex. 16, col. 21, lines 54-57) and other biologically active substances (Ex. 13, col. 21, lines 6-7). Therefore, Cook et al. teach all of the elements of claims 1, 2, 4-6, 8, 10 and 15.

Art Unit: 1653

The applicant argues that Cook et al does not describe two layers that comprise cross-linking. However, Cook et al. does describe a first cross-linked layer and a second layer, for example, human bone morphogenetic protein-2 (see claim 21), that comprises cross-linking as it is cross-linked to a cross-linking agent (col. 8, lines 1-10). Claim 1 does not include a limitation that each layer has cross-linking within itself.

Claims 1, 2 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Schwartz et al. (United States Patent Number 5,906,997) teach a biodegradable (col. 3, line 55) multilayer (col. 3, lines 48-50) cross-linked (col. 7, lines 53-57) matrix comprised of the polysaccharide chitin, chitosan, hyaluronic acid, heparin, heparan sulfate, chondroitin sulfate (col. 6, lines 63-67). Thus, Schwartz et al. teach all the elements of claims 1, 2 and 5.

The applicant argues that Schwartz et al. do not teach a multi-layer matrix but rather teaches one layer and this layer does not contain any cross-linking. However, Schwartz et al. specifically teaches that the amount of cross-linking in the layer may be increased or decreased by adjusting the pH (col. 7, lines 50-55) and therefore there is at least some cross-linking. Schwartz et al. further teach that “[m]ulti-layered membranes are also an aspect of this invention.” (col. 3, lines 48-51).

Claims 1-6, 8, 10, 11, 13, 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Yannas (United States Patent Number 4,902,289). Yannas teaches a multi-layer matrix comprising two layers comprised of covalent (col. 3, line 26) cross-linked collagen (col. 3, line 9) and where the polysaccharide for both layers is selected from any of the following and need not be identical to each other: chondroitin sulfate, heparan sulfate, dermatan sulfate, keratan sulfate, heparin, hyaluronic acid, or chitosan (claim 3). Yannas teaches that each layer

Art Unit: 1653

of the matrix is chemically crosslinked by glutaraldehyde to each other (col. 7, lines 15-18) and the porosity of the first layer is less than 10 microns (col. 6, lines 34-35), of the second layer is 50 microns or greater (col. 7, line 29) and where the first layer comprises collagen and elastin cross-linked to each other (Ex. 2, col. 9, lines 55-60). Thus, Yannas teaches all the elements of claims 1-6, 8, 10, 13, 15 and 16.

The applicant argues that Yannas et al. do not teach "a polysaccharide cross-linked to collagen" (amendment p. 3, lines 19-20), that no layer disclosed in Yannas et al. is a cross-linked protein or polysaccharide and that the coating in Yannas et al. is used on a blood vessel prosthesis and is not directed to tissue regeneration and therefore does not anticipate the claims. However, Yannas teaches that covalent "cross-linking anchors the aminopolysaccharide chains to the collagen" (col. 3, lines 25-30). Further, the claims of the present invention are not method claims for tissue regeneration and as Yannas et al. teaches all the elements of the composition in claims 1-6, 8, 10, 11, 13, 15 and 16, these claims are anticipated under 35 U.S.C. 102(b).

Claims 1, 6 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Boyce (United States Patent Number 5,273,900) teaches a cross-linked dermal membrane comprising collagen and chondroitin sulfate (Ex. 1, col. 12, line 47) where said layers are chemically cross-linked to each other with glutaraldehyde (col. 7, lines 59-62) and also are cross-linked by thermal dehydration (col. 7, line 53). Thus, Boyce teaches all the elements of claims 1, 6 and 18.

The applicant argues that Boyce teaches layers of collagen cross-linked to a polysaccharide. Boyce therefore teaches protein layers that comprises cross-linking as it is cross-linked to a polysaccharide and the (col. 8, lines 1-10). Claim 1 does not include a

Art Unit: 1653

limitation that each layer has cross-linking within the protein itself or within the polysaccharide itself, but merely that each layer comprises cross-linking.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8, 9, 12, 14, 15, 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hook et al. (United States Patent Number 4,784,989) and Liu et al. (United States Patent Number 5,972,385) in view of Schwartz et al. Hook et al. teach a cross-linked polymeric component comprising fibrinogen, fibronectin, albumin, collagen or laminin (col. 2, lines 62-65) and dextran or alginate (col. 3, lines 3-5) wherein the crosslinking agent is divinyl sulfone (col. 3, lines 10-15). Liu et al. teach a cross-linked polymeric component comprising hyaluronic acid, chondroitin sulfate, dermatan sulfate, keratan sulfate, heparin, heparan sulfate, dextran, dextran sulfate or alginate and collagen (col. 2, lines 26-31) and/or fibrinogen (col. 2,

Art Unit: 1653

line 66). Neither Hook et al. nor Liu et al. teach a multi-layered matrix for use in tissue regeneration. Schwartz et al. teach the advantages of using a multi-layered matrix (Schwartz et al., col. 2, line 61) to manipulate the components and ingredients in each layer resulting in each layer exhibiting different properties as desired (Schwartz col. 3, lines 47-50). It would have been obvious to one of ordinary skill in the art at the time of the invention by applicant to add a second layer comprised of the proteins and polysaccharides listed above used by Hook or Liu, of either the same components as the first layer or different components from the lists above yielding a second layer of different composition and density, and which is crosslinked with divinyl sulfone, an agent known by Hook to bond these components (col. 3, lines 12), in order to be able to manipulate the components and concentrations of each layer to yield more control and flexibility in the properties exhibited.

The applicant argues that Hook et al. does not render the claims obvious as Hook et al. does not teach a protein that is cross-linked within itself and that is used in tissue regeneration. This argument is unpersuasive as the claims are not method claims but rather are drawn to a composition comprising a bi-layer matrix comprising cross-linking components in each layer and with no limitation that the protein must be cross-linked to itself. As Hooke et al. teach a layer comprising protein cross-linked by the cross-linking agent divinyl sulfone, Hooke et al. establishes that divinyl sulfone is useful as a cross-linking agent to a protein. The applicant also argues that there is no motivation to combine the references of Hook et al., Schwartz et al. and Liu et al. However, Liu et al. does teach a matrix useful for the field of tissue regeneration. Liu et al. teaches the advantages of using a matrix comprising a cross-linked polymeric component comprising hyaluronic acid, chondroitin sulfate, dermatan sulfate, keratan sulfate, heparin,

Art Unit: 1653

heparan sulfate, dextran, dextran sulfate or alginate and collagen (col. 2, lines 26-31) and/or fibrinogen (col. 2, line 66) for the growth of tissue (see abstract). And since Schwartz et al. teach the advantages of using a multi-layered matrix (Schwartz et al., col. 2, line 61) to manipulate the components and ingredients in each layer resulting in each layer exhibiting different properties as desired (Schwartz col. 3, lines 47-50) and Hooke et al. teach that divinyl sulfone is a useful cross-linking agent, it would have been obvious to one of ordinary skill in the art at the time of the invention by the applicant to combine the related and useful teachings of each to make a bi-layer cross-linked matrix that may be used in tissue regeneration.

### ***Conclusion***

**No claims are allowed.**

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.



Art Unit: 1653

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laurie Mayes whose telephone number is (703) 605-1208. The examiner can normally be reached on flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1123.



Laurie Mayes  
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Art Unit 1653



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